Identification of radical intermediates in the hypochlorite- induced fragmentation of mono- and poly-saccharides

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Activation of leukocytes both *in vitro* and in chronic inflammatory conditions results in the release of the heme enzyme myeloperoxidase (MPO) and the formation of H_20_2. MPO catalyses the production of HOCl from H_20_2 and Cl^-. We have previously demonstrated that reagent HOCl reacts with the polysaccharides that form extracellular matrix to generate polymer-derived *N*-chloramides. Subsequent decomposition of these species results in radical formation and polymer fragmentation. Evidence has been presented for the involvement of nitrogen-centred radicals, though the mechanism of fragmentation is incompletely understood. In the present study, we have examined the radical intermediates generated from key mono-saccharides and derivatives by EPR spin trapping.

Decomposition of *N*-chloramides formed from *N*-acetyl glucosamine gave spectra consistent with the trapping of a C-2 carbon-centred radical; the identity of this species was confirmed by ^{13}C-labelling. This radical has been shown to arise via a novel rapid intra-molecular hydrogen atom 1,2-shift to an initial nitrogen-centred radical. The corresponding C-1 alkyl glycosides gave spectra consistent with the trapping of both C-2 carbon-centred radicals and carbon-centred radicals formed on the glycosidic alkyl group, with the latter formed via intra-molecular 1,5-shift reactions. The trapping of C-2 carboncentred radicals with these glycosides was found to be pH-dependent consistent with the occurrence of acid- and base-catalysed rearrangements. Studies under both anaerobic and aerobic conditions suggest that both these carbon-centred radicals, and subsequent peroxyl species can give rise to
strand scission.